Exploring the regulatory mechanisms of IL-22 in intestinal repair and mRNA-based therapeutic strategies

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Abstract

Inflammatory bowel disease (IBD) is a chronic and relapsing inflammatory disorder of the gastrointestinal tract, primarily including Crohn's disease and ulcerative colitis. Its pathogenesis is largely associated with exaggerated immune responses to the gut microbiota, leading to disruption of the intestinal mucosal barrier and resulting in symptoms such as abdominal pain, diarrhea, and intestinal bleeding. IL-22 is a key cytokine involved in innate immune regulation, with functions that include promoting epithelial cell proliferation, maintaining mucosal integrity, and modulating antimicrobial defense. This report integrates findings from two studies. The first investigated the regulatory mechanisms of IL-22 in intestinal epithelial repair and mucosal defense, while the second developed an oral lipid nanoparticle delivery system for IL-22 mRNA and evaluated its therapeutic potential in ulcerative colitis. Results show that IL-22 enhanced the growth and proliferation of human colon–derived intestinal organoids, upregulated membrane-bound mucins, antimicrobial peptides (AMPs), and Reg family genes, while downregulating goblet cell–associated genes. In *in vivo* experiments, oral administration of IL-22 mRNA–loaded lipid nanoparticles significantly reduced the expression of lipocalin-2, IL-1β, IL-6, and TNF-α in the DSS-induced colitis mice, alleviating inflammation and promoting mucosal repair. Together, these studies demonstrate the anti-inflammatory and epithelial-restorative effects of IL-22, highlighting its therapeutic potential in the regulation and treatment of intestinal inflammatory disorders.

Reference

Junsik Sung, Zahra Alghoul, Dingpei Long, Chunhua Yang, Didier Merlin. Oral delivery of IL-22 mRNA-loaded lipid nanoparticles targeting the injured intestinal mucosa: A novel therapeutic solution to treat ulcerative colitis. *Biomaterials*, 2022, 288, 121707.

Lori Patnaude, Martha Mayo, Regina Mario, Xiaoming Wu, Heather Knight, Kelly Creamer, Sarah Wilson, Valerie Pivorunas, Jozsef Karman, Lucy Phillips, Robert Dunstan, Rajesh V. Kamath, Bradford McRae, Sonia Terrill. Mechanisms and regulation of IL-22-mediated intestinal epithelial homeostasis and repair. *Life Sciences*, 2021, 271, 119195.